

## **Section: Contact Information**

First Name : **John**  
Last Name : **Groarke**  
Institution : **Brigham & Women's Hospital**  
Address 1 : **75 Francis Street**  
Address 2 :  
City : **Boston**  
State/Province/Region : **MA**  
Country : **US**  
Zip/Postal Code : **02115**  
Phone Number : **7817424782**  
Alternate Phone Number :  
Email Address : [jgroarke@bwh.harvard.edu](mailto:jgroarke@bwh.harvard.edu)

## **Section: Project Requirements and Description**

### ***Group: Requirements to submit AOI***

A comprehensive review of previously published data has been completed. : **Yes**

The specific aims are clear and focused. : **Yes**

The investigator has appropriate experience and expertise to develop the concept proposal; if not, has identified a mentor or senior co-investigator. : **Yes**

The investigator agrees to develop an initial draft of the concept proposal within 6 weeks of approval of the AOI and to finalize the concept proposal within 6 months. : **Yes**

Project Title : **Cardiovascular autonomic dysfunction as a late treatment effect in long term survivors of childhood cancer.**

Planned research population (eligibility criteria) :

**A cross-sectional study of 5 cohorts with 100 subjects in each cohort: cisplatin cohort, vincristine cohort, cranial irradiation cohort, chest radiation cohort, and sibling control cohort. All subjects will already be enrolled in the Childhood Cancer Survivor Study. Survivors in each cohort will be within 10-15 years of exposure, and exposure will have occurred between the age of 10-20 years.**

Proposed specific aims :

**Specific aim 1: To estimate the prevalence of cardiovascular autonomic dysfunction (AD) in adult survivors of childhood cancer treated with cisplatin, vincristine, cranial irradiation, or chest radiation therapy, compared to sibling controls. We hypothesize that childhood cancer survivors with remote exposures to either cisplatin, vincristine, cranial radiation, or chest radiation demonstrate a higher prevalence of autonomic dysfunction compared to sibling controls, with varying effect size.**

**Specific aim 2: To assess potential functional implications of cardiovascular autonomic dysfunction among survivors of childhood cancer. We hypothesize that cardiovascular autonomic dysfunction is associated with exercise limitation and fatigue in childhood cancer survivors.**

Will the project require non-CCSS funding to complete? : **Yes**

If yes, what would be the anticipated source(s) and timeline(s) for securing funding? :

**This project will be the basis for a National Institutes of Health developmental research grant award (R21) that will be submitted for the February 2019 grant deadline cycle.**

***Group: Does this project require contact of CCSS study subjects for:***

Additional self-reported information : **Yes**

Biological samples : **No**

Medical record data : **No**

If yes to any of the above, please briefly describe. :

**ADDITIONAL SELF-REPORTED INFORMATION:** Subjects will be asked to complete a self administered questionnaire that will assess the following components:

- Height in inches, weight in pounds (ideally from within 1 month of participation)

- List of current medications

- Smoking status

- Physical activity assessment: using the World Health Organization Global Physical Activity Questionnaire (GPAQ). The GPAQ comprises 16 items that quantify the physical activity levels of a normal active week during work, transit, and leisure time. Depending on cost, a similar alternative questionnaire may be used.

- Fatigue: using the Functional Assessment for Cancer Therapy-Fatigue scale (FACIT Fatigue scale) which is a 13 item instrument designed to assess fatigue and its impact on daily activities and functioning in a number of chronic diseases. Depending on cost, a similar alternative questionnaire may be used.

- Exercise capacity: using the Duke Activity Status Index, a self-administered questionnaire comprising 12 questions for estimating functional capacity. Depending on cost, a similar alternative questionnaire may be used.

**BIOLOGICAL SAMPLES:** No blood/tissue samples will be required for this study. Rather, heart rate data will be continuously recorded over at least 24 consecutive hours using a non-invasive wearable wrist monitor. This will allow for remote monitoring.

**Group: What CCSS Working Group(s) would likely be involved? (Check all that apply)**

Second Malignancy :

Chronic Disease : **Secondary**

Psychology / Neuropsychology :

Genetics :

Cancer Control : **Primary**

Epidemiology / Biostatistics : **Secondary**

### **Section: Outcomes or Correlative Factors**

Late mortality :

Second Malignancy :

**Group: Health Behaviors**

Tobacco :

Alcohol :

Physical activity : **Secondary**

Medical screening :

Other :

If other, please specify :

**Group: Psychosocial**

Insurance :

Marriage :  
Education :  
Employment :  
Other :  
If other, please specify :

**Group: Medical Conditions**

Hearing/Vision/Speech :  
Hormonal systems :  
Heart and vascular : **Primary**  
Respiratory :  
Digestive :  
Surgical procedures :  
Brain and nervous system :  
Other :  
If other, please specify :

**Group: Medications**

Describe medications :

**Group: Psychologic/Quality of Life**

BSI-18 :  
SF-36 :  
CCSS-NCQ :  
PTS :  
PTG :  
Other : **Secondary**  
If other, please specify : **Fatigue**

**Group: Other**

Pregnancy and offspring :  
Family history :  
Chronic conditions (CTCAE v3) : **Correlative Factors**  
Health status :

**Group: Demographic**

Age : **Correlative Factors**  
Race : **Correlative Factors**  
Sex : **Correlative Factors**  
Other :  
If other, please specify :

**Group: Cancer treatment**

Chemotherapy : **Correlative Factors**  
Radiation therapy : **Correlative Factors**  
Surgery :

**Section: Anticipated Sources of Statistical Support**

CCSS Statistical Center : **Yes**

Local institutional statistician :

If local, please provide the name(s) and contact information of the statistician(s) to be involved. :

Will this project utilize CCSS biologic samples? : **No**

If yes, which of the following? :

If other, please explain :

### **Section: Other General Comments**

Other General Comments :

**Cancer, certain cancer drugs, radiation therapy, cancer-associated lifestyle disturbances, and cancer-independent comorbidities combine to predispose cancer survivors to autonomic dysfunction (AD). Elevated resting heart rate (HR) and reduced HR variability (HRV) have been described in various cancer cohorts. Furthermore, these markers of AD have been implicated in adverse outcomes in oncology patients, including increased mortality, exercise limitation, and fatigue. However, data are largely derived from small studies with methodological limitations, and the contribution of AD to overall morbidity in cancer survivors is not well understood. Thus we propose this project which will utilize a wearable wrist monitor for remote assessment of resting heart rate and heart rate variability to investigate the specific aims described above.**

I agree to share this information with St. Jude : **Yes**